

## EXOGENOUS LIPOID PNEUMONIA (OIL GRANULOMAS OF THE LUNG)

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The authors observed three cases of exogenous lipid pneumonia clinically suspected of lung carcinoma. Histological examination of material after thoracotomy gave the possibility of correct diagnosis. The lesions in lungs were characteristic granulomas around lipid material and with surrounding advanced fibrosis.

**Key words:** oil granulomas of lung, lipid lesions of lung, foreign body granulomas, non-neoplastic tumours of lung.

Lipid pneumonia of exogenous origin is an uncommon disease resulting from aspiration or inhaling oils [1-6]. The source of oil in adults can be from nose oil drops or laxatives. Vegetable, mineral and animal oils produce different morphological changes. Vegetable oils are not hydrolysed by lung lipase and are mostly expectorated with small damage in the lung. Contrary to that, animal oil can be hydrolysed and liberate fatty acids promoting severe inflammation [1]. In children lipid pneumonia is more frequent and often is connected with a defect in the palate and also many years ago with cod liver oil, milk fat and egg yolk. Also many years ago lipids were used as drugs put into the bronchi or as contrast material in radiological examination and were the aetiological agent of lipid pneumonia. There are sometimes occupational exposure cases of exogenous lipid pneumonia.

Because of the rarity of this entity, many clinicians are unfamiliar with it. Patients are asymptomatic or present non-specific symptoms (fever, weight loss, cough, dyspnoea, abundant sputum, chest pain, haemoptysis) [7] and only chest X-ray examination shows lesions in the lungs, mimicking other diseases, mainly neoplasm in older patients. For the pathologist these lesions in a lungs are also very strange and unusual.

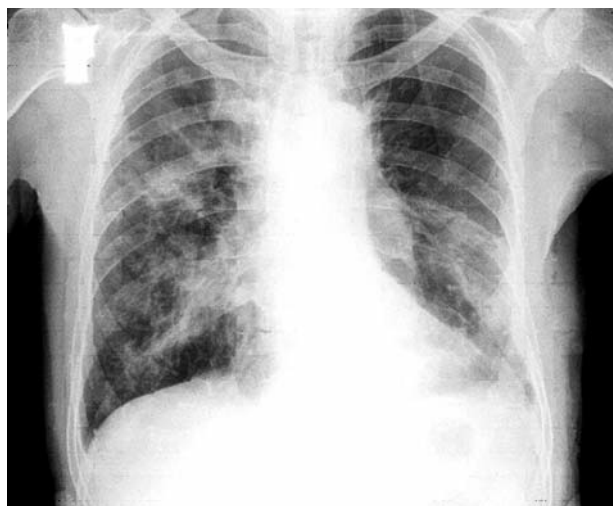
During the last eight years we have had the opportunity to observe three cases of oil granulomas of the lung connected with use of exogenous oil as medicaments, orally or by nose.

### Report of cases

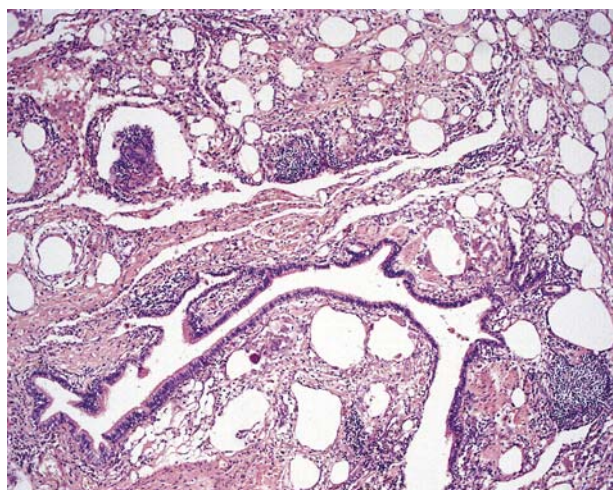
#### Case 1

Man JJ, 67 years old, case No. 130696-1529449, a teacher, an oil drinker. He has had bronchitis and laryngitis for many years. He used inhalant drugs. Suspected of tuberculosis because of lesions in chest X-ray and lung carcinoma because of blood in sputum (Fig. 1). He has also had arterial hypertension and cardiac insufficiency. In 2003 a computed tomography scan showed consolidations located in posterior parts of both lungs, more advanced in the left. In bronchofibroscopy left bronchi 6 and 9 were narrowed, left 10 bronchus was occluded, but histopathology of small pieces of bronchial tissue was inconclusive. At this time there was a little fluid in the pericardium. Spirometry: FEV1 1700 ml – 52%, FVC 2750 ml – 62%, FEV1/FVC – 61.99%. In November 2003 thoracotomy was performed. A tumour 3-4 cm in diameter from the sixth segment of the left lung which infiltrated the adjacent lung, mediastinum and descending aorta was partially removed. After surgery patient status was good. He died two years later because of pneumonia; no autopsy was performed.

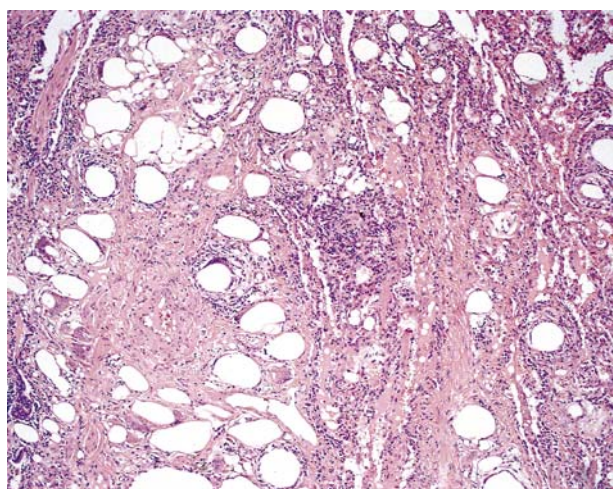
Material fixed in 10% buffered formalin was embedded in paraffin blocks and next used for slides stained with HE.



**Fig. 1.** Case 1. Chest X-ray. Many tumour-like consolidations in both lungs are seen



**Fig. 2.** Part of tumour with empty spaces after dissolved fat. Multinucleated foreign body cells, on their margin empty places. Structure of lung totally distorted, also visible fibrosis. Case 1

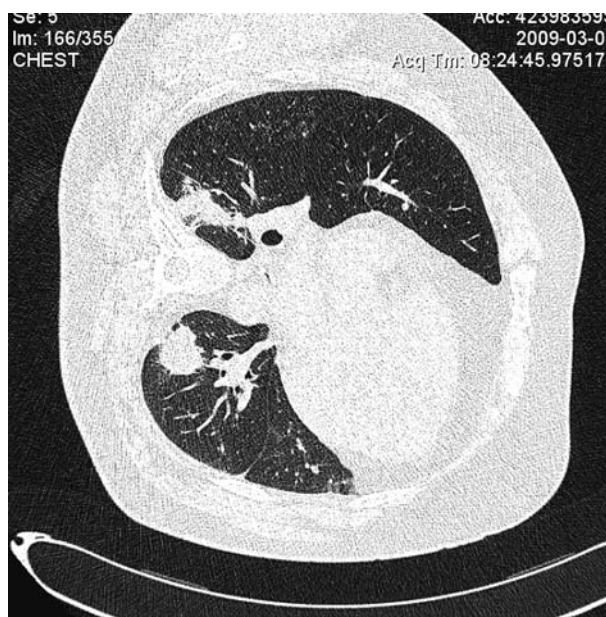


**Fig. 3.** Typical picture of oil granuloma with local advanced fibrosis of lung. Case 1

In the lung instead of normal alveoli there were empty spaces larger and smaller than normal alveoli, lined with partially flattened multinucleated giant cells (Fig. 2). In frozen section in these empty places observed in slides after paraffin embedding there were lipids stained with Sudan III. Among those empty places loose fibrous connective tissue and proliferated fibroblasts were seen, sometimes with infiltration of lymphocytes forming lymphatic follicles, some with germinal centres. In connective tissue there were also foreign body granulomas with large multinucleated cells which had lipid in the cytoplasm (Fig. 3). The bronchiole in the vicinity had a widened lumen and signs of chronic inflammation in the walls. The arteriole had a narrowed lumen and thickened, partially hyalinized wall and proliferated smooth muscles. The lesions did not have a distinct margin with the normal lung.

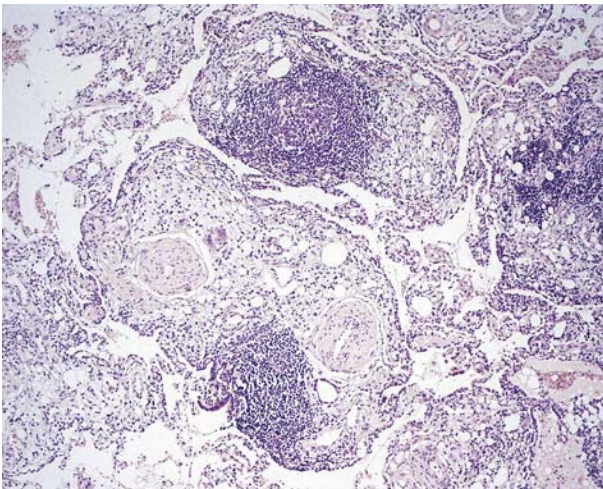
## Case 2

Man KM, 47 years old, parquet worker, in his work used chemicals (Subit, Drewnolux, Hemolak), heavy alcohol drinker, treated with antidepressant drugs during psychiatric therapy. In 2008 chest X-ray examination showed several tumours to a few centimetres in diameter in peripheral parts of lungs. In computed tomography with contrast it was adequate to soft and fat tissue. The margin of lesions was irregular with spicules. Hilar and mediastinal lymph nodes were of normal sizes (Fig. 4). Spirometry: FEV1 2610 ml – 72.9%, FEC 3190 ml – 73%, TEV1/FVC – 102.9%. Thin needle biopsy was negative. Surgeons decided to perform left side thoracotomy and removed one tumour for histopathological examination. After the surgery, the current patient's status was good.



**Fig. 4.** Computed tomography scan shows tumours in paravertebral regions of both lungs. Case 2



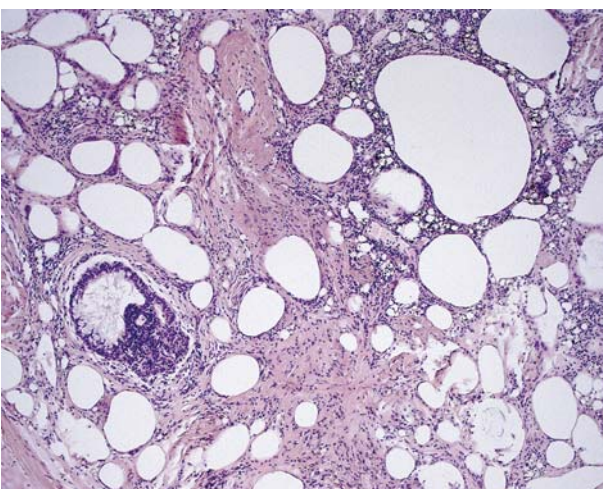


**Fig. 5.** Oil granuloma in case 2. There are nodular foci of lymphocytes and thickened walls of blood vessels with proliferation of smooth muscles and narrowed lumen

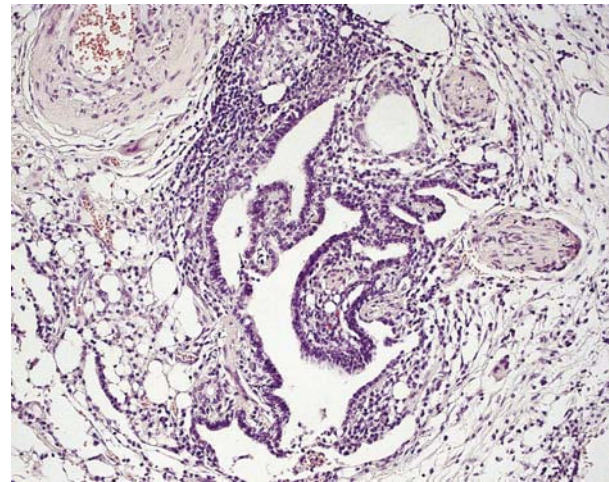
Histopathological slides No. 192634 showed a picture similar to the first case, but there was more fibrous tissue and arteriolar wall changes were more pronounced (hyalinisation, proliferation of smooth muscle and narrowed lumen). Also the arteriolar adventitia was more abundant (Figs. 5 and 6).

### Case 3

Man KI, 73 years old, opera singer, native Georgian. For 50 years because of common laryngitis and bronchitis he had used a mint oil which he had put on the tongue and aspirated to the lung. After this procedure he coughed up and his voice was better. A Georgian laryngologist also cured him with locally used oils. In April 2009 chest X-ray showed lesions in lungs. Spirometry was as follows: FEV1 3030 ml – 113%,



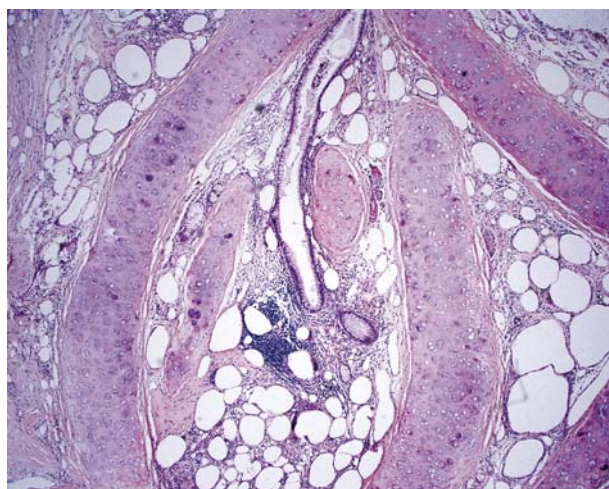
**Fig. 7.** Many multinucleated giant cells on margin of fat and local fibrosis of lung. Case 3



**Fig. 6.** Thickened wall of blood vessel with hyalinisation. Many droplets of fat in vicinity of bronchus. Case 2

FVC 3860 ml – 111%, FEV1/FVC – 78.50%. Computed tomography revealed parenchymal infiltrations with irregular borders, a few centimetres in diameter in peripheral parts of the lungs. In contrast examination it was adequate to soft and fat tissues. Bronchi in these regions were partially compressed. Hilar and mediastinal lymph nodes were of normal size. Left side thoracotomy was performed and the lower lobe with a 3 cm tumour in it was removed. Material was fixed in formalin and embedded in paraffin blocks (No. 196765-6, 196799). After surgery and for the next several months the patient's status was good.

In this case lesions in the lung were more severe than in the first and the second cases (Fig. 7). There was more collagen with its pressure on bronchi with their narrowing and deformation, in a fashion similar to inborn lesions (Fig. 8). Areas with abundant collagenisation



**Fig. 8.** Narrowed lumen of large bronchus pushed by fat around and gathered droplets of fat in bronchial mucosa. Also fibrotic tissue and hyalinization in old granulomas caused distorted architecture of bronchus. Case 3

(with no cells) underwent hyalinisation and calcification. In other fields lesions have a similar appearance as in the first two cases.

## Discussion

Pathologists often observe lipid pneumonia of endogenous origin in surgical material and autopsies, usually connected with neoplasm narrowing the bronchi; we call it obstructive pneumonia. This lipid is mainly of surfactant origin which normally is recycled by the alveolar epithelium and partially removed through the bronchi. Bronchial local stenosis is connected with accumulation of phagocytes (alveolar macrophages) which have abundant clear cytoplasm and fill lung alveoli. This lipid material is osmophilic, and is intracellular, and no giant cell reaction is observed except around cholesterol crystals [3]. Other cases of endogenous lipid pneumonia are connected with pulmonary alveolar lipoproteinosis, therapy (some drugs, for example amiodarone) or inherited gene defects disease (e.g. Niemann-Pick disease).

In exogenous lipid pneumonia we can find in the lung mostly mineral saturated, non-osmophilic oil (paraffin) used as a vehicle for nasal drugs. The gathered oil provokes a granulomatous inflammatory reaction with many macrophages and giant cells. Droplets of oil have a tendency to coalesce and to fill alveoli totally, but this material during embedding in paraffin blocks is removed and on slides we have only empty places. On frozen section we have a possibility to stain this oil (Sudan black, Sudan red and others).

Wagner *et al.* [8] suggested four stages in pathogenesis of oil granulomas in the lung:

Stage I is observed in infants who died with asphyxia after inhalation of milk. Morphologically, fat milk is observed in bronchi and bronchioles and alveoli are surrounded by scanty neutrophils, lymphocytes and occasionally giant cells.

Stage II is the absorption of lipids and subsequent foreign body reaction. Numerous macrophages in alveoli absorb fat and oil but also are present in lymphatic vessels. Foamy cytoplasm of macrophages sometimes contain needle-shaped crystals. The wall of alveoli is thickened with collagen fibres and sometime with proliferation of fibroblasts. Inflammatory infiltration contains lymphocytes, plasma cells and occasionally giant cells. Also in these cells perivascular fibrous tissue is increased. In bronchi and bronchioles epithelial cells are swollen.

Stage III – it is the stage when we can see elastic tissue degeneration and endarteritis. Alveoli are distorted and many of them are collapsed. Lymphocytes and plasma cells have disappeared from alveoli; now they only contain phagocytes, multinucleated giant cells and desquamated alveolar epithelial cells. In the alveolar wall there is a large amount of reticulin and the cap-

illaries are completely replaced by collagen fibres and fibroblast. The architecture of the lung is distorted. Sometimes foci of multinucleated giant cells are surrounded by palisading epithelioid cells in a similar manner to those in tuberculosis. In arterioles, the normal adventitia and media are replaced by fibrous tissue. In all layers numerous small vacuoles containing oil can be seen and in these places elastic fibres are fragmented. The lumen of vessels is reduced. Similar lesions are observed in bronchi except the lumen, which is enlarged and of bronchiectatic appearance. Lymphatic tissue of the lung is hyperplastic with lymphocytic aggregation around oil globules.

Stage IV – it is increasing fibrosis with progressive endarteritis. Elastic tissues of arterioles, bronchi and bronchioles are replaced by a reticulum network. Bronchi are collapsed and arterioles occluded. On dense fibrous tissue we can see hyaline degeneration or necrosis. In the authors' opinion at any one of these stages the infection can distort the histological appearance.

All our three cases can belong to stages III and IV in Wagner's classification.

In recent medical literature there are only a few case reports of oil granulomas in the lung [9-17]. In a paper by Spickard and Hirschman [11] one can find detailed information about methods of administration of fat to the lung connected with customs around the world.

We have found one paper of a multicentre study from France of 44 cases of exogenous lipid pneumonia [7]. Those were 4 cases of occupational diseases and 30 cases connected with use of liquid paraffin for the treatment of constipation. Twenty-four cases were submitted for histological examination. In the remaining cases diagnosis came from clinical and radiological observations.

It is discussed whether bronchoalveolar lavage (BAL) can be useful in diagnosis, or perhaps may only confirm clinical, radiological and histological diagnosis by presence of many lipophages. However, for Gonduin *et al.* [7] BAL was highly suggestive in 30 cases. Bronchoalveolar lavage examination showed in those cases lymphocytic alveolitis, neutrophilic alveolitis and mixed alveolitis. Specific stains for fat and milky, oily and haemorrhagic BAL fluid can complete the diagnosis. Launge *et al.* [18] had a similar opinion. Silverman *et al.* [19] questioned the usefulness of the BAL method in diagnosis of lipid pneumonia. In their opinion, this method may be preferred only for confirmation of lipid pneumonia, thereby avoiding invasive procedures.

Lipid granulomas were also observed in the lungs of a patient after radical surgery because of carcinoma of the larynx (personal communication Dr R. Langfort – Institute of Tuberculosis and Pulmonary Diseases, Warsaw, Poland).

For chemical differentiation of fat, osmic acid which stains animal and plant fat (not mineral) can be

used. It result of unsaturated fats absent in mineral oil. Other chemical and technical methods were also used.

We suppose that in future there will be fewer cases of oil granulomas in the lung also in our country as well as in western European countries and USA. It will result in less use of oil vehicle for drugs and other laxative drugs than today. It is necessary to teach medical staff and other citizens about the risks connected with using oils.

There is no successful therapy in this disease. When we stop using lipids, tumours in the lung will not grow; it is just contrary to any neoplasms. In some advanced cases, transplantation of lungs may be considered.

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